REMARKS

These remarks are in response to the Final Office Action mailed March 15, 2001. Claims 1-7 have been canceled without prejudice or disclaimer, and claims 8-14 have been added. The new claims are supported in the specification and claims as filed, hence no new matter has been added.

A Petition to Revive the above identified application, a Request for Continued Examination, and a Petition for an Extension of time are also attached.

I. Amendments to the Claims

New claims 8-14 have been added. New claims 8-14 have support in the specification and claims as filed, for example, in Examples 1-6 and Tables 2 and 3.

The new claims are directed to amino acid sequence as set forth in SEQ ID NO:2. The claims which were cancelled were directed to SEQ ID NO:5. The amino acid sequence of SEQ ID NO:2 is entirely incorporated within SEQ ID NO:5 (see Table 2 and Example 3, p.28, line 16).

Hence, no new matter has been added in new claims 8-14.

II. Rejection under 35 U.S.C. §112, first Paragraph

Claims 1-7 are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification. Applicants respectfully traverse this rejection.

Claims 1-7 have been cancelled, thus making the rejections to claims 1-7 moot. However, claims 8-14 have been added, thus the following discussion will address the rejection as they relate to claims 8-14.

The Office rejects the claims based on two grounds, alleged lack of a written description and enablement. These are separate rejections and are addressed individually below.

A. Rejection under 35 U.S.C. §112, first paragraph, written description

According to the Office Action, the claimed invention is allegedly not described in the specification because HBGF is a sub-fragment of the longer protein, CTGF, and it would therefore not be predictable that an antibody to the HBGF fragment would produce novel epitopes such that antibodies to HBGF do not cross-react with that of CTGF (see page 3, third

paragraph). Also, according to the Office Action, Lerner teaches away from Applicants claim that novel epitopes are possible and not undue (Lerner, *Nature* 299: 592, 1982). Applicants respectfully traverse this rejection.

Briefly, the specification fully and clearly describes the metes and bounds of the claimed invention. For example, Example 1 describes purification of HBGF polypeptides that are about 10 kDa (page 22, line 3-4). Example 2 describes the N-terminal sequencing of the isolated HBGF polypeptides, resulting in two HBGF polypeptides which were N-terminally identical except for the presence of an additional glutamic acid (Glu) at the N-terminus of one of them (p.26, lines 7-9). The sequences of these polypeptides are shown in Table 2 (SEQ ID NO:1 and 2). SEQ ID NOs: 1 and 2 align to internal regions of human and mouse CTGF at amino acids 247 or 248 to 349 of CTGF (the deduced CTGF sequence is a 349 amino acids). Hence, HBGF polypeptides are "microheterogenous forms of truncated CTGF" (see p.28, line 10). Example 3 provides methods of making an antibody against SEQ ID NO:5 (EENIKKGKKCIRTOP) corresponding to amino acid residues 247-260 of CTGF (p.28, line 16). Example 4 shows that the antibody against SEQ ID NO:5 is immunoreactive to the predicted 10 kDa proteins, but is also immunoreactive to 16 and 20 kDa proteins (p.29, line 17). The antibody was *not* immunoreactive to a 38 kDa protein; hence, the 10 to 20 kDa proteins are not break-down products of the 38 kDa protein (p.29, line 24-25); because if they were, the antibody described would have cross-reacted with the 38 kDa protein.

So, although Lerner (1984) discloses that various monoclonal antibodies raised against *isolated peptides* from influenza virus do cross-react to both the peptide and the whole virus, this is not a universal phenomenon, otherwise there would be no need for monoclonal antibodies with increased specificity. In fact, Applicants submit that one of ordinary skill in the art would acknowledge that whether antibody cross-reacts to a protein is dependent on the antigenic properties of individual proteins or peptides.

For example, CTGF and PDGF are only 40% identical and are products of different and distinct genes. Yet, CTGF and PDGF are still related immunologically (antigenically) and

biologically (see col. 1, lines 62-64; col. 2, lines 33-35; and col. 3, lines 45-47 of U.S.P.N. 5,408,040 to Grotendorst; hereinafter, "Grotendorst"). The primary subject matter of Grotendorst is an approximately 36-38 kDa CTGF polypeptide (col. 2, lines 63-65); and as discussed above, the claimed antibody is not immunoreactive to the 36-38 kDa CTGF polypeptide.

Thus, the claimed invention *can* and *does* produce novel epitopes capable of recognizing the corresponding 10 kDa protein, as well as a 16 and 20 kDa protein, which are *not* break-down products of the 36-38 kDa CTGF protein; because the antibody does *not* cross-react to a polypeptide of that approximate molecular weight (i.e., 36-38 kDa). Therefore, the application as filed provides a full, clear, concise and exact description for making and using an antibody to SEQ ID NO:5. Further, since SEQ ID NO:2 is fully incorporated within SEQ ID NO:5, the application as filed describes a full, clear, concise and exact description for making and using an antibody to SEQ ID NO:2 as well.

Accordingly, withdrawal of rejection of the claims under 35 U.S.C. § 112, first paragraph is respectfully requested.

B. Rejection under 35 U.S.C. §112, first paragraph, enablement

According to the Office Action, the claimed invention allegedly does not satisfy the enablement requirement and would amount to undue experimentation on the part of one skilled in the art. Applicants respectfully traverse this rejection.

The Office Action states that the 8 factors of *In re Wands* are not satisfied. *In re Wands,* 858 F.2d 731, 737, 8 USPQ 1400, 1404 (Fed. Cir. 1988). The eight factors considered are: 1) nature of the invention; 2) state of the prior art; 3) relative skill of those in the art; 4) level of predictability in the art; 5) existence of working examples; 6) breadth of claims; 7) amount of

direction or guidance by the inventor; and 8) quantity of experimentation needed to make or use the invention. *In re Wands,* supra.

The nature of the invention are HBGF antibodies to a 10 kDa protein having amino acid sequence as set forth in SEQ ID NO:2. The level of skill is high, but no higher than other related fields of molecular and biochemistry. One of ordinary skill in the art would predict that an antibody to SEQ ID NO:2, which is fully incorporated into SEQ ID NO:5, would specifically cross-react to a 10-20 kDa protein(s) and not cross-react to a 36-38 kDa protein, and thereby specifically binding to an HBGF polypeptide (discussed above). Examples 1-6 present clear working examples of how to carry out the metes and bounds of the claimed invention (discussed above). Hence, the breadth of the claims are well within the description of the application as filed, and there is sufficient guidance provided to one of ordinary skill in the art at the time of filing without undue experimentation.

Accordingly, withdrawal of rejection of the claims under 35 U.S.C. § 112, first paragraph is respectfully requested.

III. Conclusion

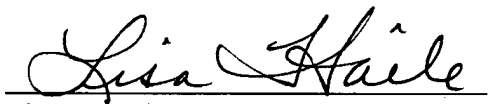
In view of the amendments and above remarks, it is submitted that the claims are in condition for allowance, and a notice to that effect is respectfully requested. The Examiner is invited to contact Applicant's undersigned representative if there are any questions relating to this application.

Applicants have attached a check for $1655.00 for Petition for Revival of an Unintentionally Abandoned Application (37 C.F.R. § 1.137(b); Request for Continued Examination and Petition for Extension of Time.

Applicants do not believe any other fees are due in connection with this submission, however if any other fees are due, please charge any fees, or make any credits, to Deposit Account No. 07-1896.

Respectfully submitted,

Date: 7/22/05



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